

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in this application.

The following amendments do not constitute an admission regarding the patentability of the amended subject matter and should not be so construed. Amendments to the claims were made for purposes of more clearly stating the claimed subject matter and do not add new matter or alter the scope of the claims.

Listing of Claims:

AMENDMENTS TO THE CLAIMS

1.-3. (Canceled)

4. (Currently Amended) A composition comprising a crystal of human growth hormone (hGH), comprising and polyarginine wherein said polyarginine is complexed with said crystal of hGH, and wherein said crystal of hGH comprises at least one cation and hGH which is selected from the group consisting of:

(a) the 191 amino acid sequence of native hGH; and

(b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine.

5.-6. (Canceled)

7. (Currently Amended) A composition comprising a crystal of human growth hormone (hGH), comprising and polyarginine wherein said polyarginine is complexed with said crystal of hGH, and wherein said crystal of hGH comprises at least one cation and hGH which is selected from the group consisting of:

(a) the 191 amino acid sequence of native hGH; and

(b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine; and

~~wherein the crystal is characterized by a release profile such that a single administration of said crystal~~ composition to a mammal provides an *in vivo* human growth hormone (hGH) serum concentration profile in said mammal having a T_{90%} value higher than that provided by a single administration of the same amount of soluble human growth hormone.

8. (Currently Amended) A composition comprising a crystal of human growth hormone (hGH), comprising and polyarginine wherein said polyarginine is complexed with said crystal of hGH, and wherein said crystal of hGH comprises at least one cation and hGH which is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine;

wherein ~~the crystal is characterized by an insulin growth factor 1 (IGF-1) serum elevation profile such that~~ a single administration of said crystal composition to a mammal provides an *in vivo* IGF-1 serum elevation over baseline IGF-1 level in said mammal at similar levels compared to those provided by the same amount of soluble human growth hormone (hGH) administered in more than one administration.

9. (Currently Amended) A composition comprising a crystal of human growth hormone (hGH), comprising and polyarginine wherein said polyarginine is complexed with said crystal of hGH, and wherein said crystal of hGH comprises at least one cation and hGH which is selected from the group consisting of

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine;

wherein ~~the crystal is characterized by a bioavailability such that~~ a single administration of said composition crystal has a relative bioavailability of at least 50% or more, as compared to that of an identical dose ~~or lower dose~~ of soluble human growth hormone (hGH) delivered via the same administrative route, wherein said bioavailability is measured by area under curve (AUC) of total *in vivo* hGH serum concentration for said soluble hGH and said hGH crystal.

10. (Currently Amended) The ~~crystal~~ composition according to claim 7 or 8, wherein said mammal is a human.

11.-16. (Canceled)

17. (Previously Presented) The composition according to claim 4, 7, 8, or 9, further comprising an additional excipient.

18. (Canceled)

19. (Currently Amended) The composition according to claim 17, wherein said additional excipient is selected from the group consisting of amino acid, a salt, an alcohol, a carbohydrate, a protein, a lipid, a surfactant, a polymer, a polyamino acid wherein said polyamino acid is not polyarginine, and mixtures thereof.

20. (Previously Presented) The composition according to claim 17, wherein said additional excipient is selected from the group consisting of protamine, polyvinylalcohol, cyclodextrin, dextran, calcium gluconate, polyamino acid wherein said polyamino acid is not polyarginine, polyethylene glycol, a dendrimer, polyorthinine, polyethyleneimine, chitosan and mixtures thereof.

21. (Currently Amended) The composition according to claim 20, wherein said additional excipient is selected from the group consisting of: protamine, ~~polyarginine~~, polyethylene glycol and mixtures thereof.

22. (Previously presented) The composition according to claim 17, wherein the concentration of human growth hormone (hGH) in said composition is between 0.1 and 100 mg/ml.

23.-62. (Canceled)

63. (Currently Amended) The composition ~~polyarginine-complexed human growth hormone (hGH)-crystal~~ according to claim 4, 7, 8 or 9, wherein the polyarginine complexed crystal is produced by:

- (a) crystallizing the hGH with a cation, and
- (b) complexing polyarginine to the crystallized ~~hGH~~.

64. (Currently Amended) The ~~polyarginine-complexed hGH-crystal~~ composition according to claim 4, ~~further comprising a cation wherein said cation is a calcium ion.~~

65. (Currently Amended) A pharmaceutical composition comprising the ~~polyarginine complexed hGH-crystal~~ composition of claim 4.

66. (Currently Amended) A pharmaceutical composition comprising the ~~polyarginine complexed hGH-crystal~~ composition of claim 7.

67. (Currently Amended) A pharmaceutical composition comprising the ~~polyarginine complexed hGH-crystal~~ composition of claim 8.

68. (Currently Amended) A pharmaceutical composition comprising the ~~polyarginine complexed hGH-crystal~~ composition of claim 9.

69.-71. (Canceled)

72. (Currently Amended) A pharmaceutical composition comprising the ~~polyarginine complexed hGH-crystal~~ composition of claim 63.

73. (Currently Amended) A pharmaceutical composition comprising the ~~polyarginine complexed hGH-crystal~~ composition of claim 64.

74. (Currently Amended) The ~~polyarginine-complexed hGH-crystal~~ composition according to claim 7, ~~further comprising a cation wherein said cation is a calcium ion.~~

75. (Currently Amended) The ~~polyarginine-complexed hGH-crystal~~ composition according to claim 8, ~~further comprising a cation wherein said cation is a calcium ion.~~

76. (Currently Amended) The ~~polyarginine-complexed hGH-crystal~~ composition according to claim 9, further comprising a cation.

Serial No.: 10/749,962
Filed: December 31, 2003

P A T E N T
WSGR Reference No. 38392-700

77.-79. (Canceled)

80. (Currently Amended) The ~~polyarginine-complexed hGH-crystal~~ composition according to claim 63, further comprising a cation.

81.-84. (Canceled)

85. (New) The composition according to claim 4, wherein said cation is a sodium ion.

86. (New) The composition according to claim 7, wherein said cation is a sodium ion.

87. (New) The composition according to claim 8, wherein said cation is a sodium ion.